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From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 15, Number 1 **January, 1950**

Announcement

Allergy Abstracts has been published since 1936 by members of the Allergy Division of the Jewish Hospital of Brooklyn. The Editorial Board is comprised of former residents of this department who contribute their services.

Allergy Abstracts selects and abstracts those articles in the literature which may be of clinical or theoretical interest to workers in the field of allergy. Each abstract represents a summary of the author's findings and views, and its inclusion in Allergy Abstracts does not imply approval of its contents by the editor. —*The Editors.*

Asthma and Hay Fever

Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm. V. Adrenergic Agents. Bresnick, E., Beakey, J. F., Levinson, L., and Segal, M. S.: J. Clin. Investigation **28**: 1182, 1949.

Vital capacity studies were made in asthmatic patients to determine the efficacy of various sympathomimetic amines in counteracting bronchoconstriction induced by histamine or methacholine. Findings in individuals varied greatly; therefore, the averages of many observations in different individuals were made the basis for comparison. Epinephrine 1:1,000, subcutaneously, protected as well or better than the other drugs despite its disagreeable side effects. Isuprel 1:100 as an aerosol was comparable to subcutaneous epi-

nephrine as an anticholinergic but protected less than half as long against histamine and also had undesirable side actions. Nebulized Vaponefrin, 2.25 per cent, protected slightly better against histamine than Isuprel 1:200 or epinephrine 1:100. Isuprel was superior to Vaponefrin as an anticholinergic. Neo-Synephrine was valueless parenterally and only slightly effective when nebulized. Isuprel in a dose of 20 mg. sublingually had little effect in counteracting either histamine or methacholine, but "was occasionally of moderate value clinically." Subcutaneously, Isuprel 1:5,000 displayed effective but brief counteraction to histamine but was less effective against methacholine. Isuprel 1:50,000, intravenously, occasionally proved dramatically effective in clinical asthma but caused palpitation and tachycardia without hypertension. Orthoxine was not thoroughly investigated. It appeared to be similar to ephedrine with the capacity to reverse the central stimulation of this drug.

Ephedrine, administered orally, afforded less than 40 per cent protection against histamine and required eighty-one minutes to attain its maximum effect, which lasted slightly over three hours. It failed to protect significantly against methacholine. The duration of effectiveness of each of the above-mentioned drugs was carefully noted and the chemical configurations of each was compared in detail. K.

Studies of Experimental Pulmonary Edema. I. Pulmonary Edema From 1-Epinephrine and 1-nor-Epinephrine (Arterenol). MacKay, E. M., and Pecka, E. F., Jr.: Proc. Soc. Exper. Biol. & Med. **71**: 669, 1949.

Unfasted guinea pigs of both sexes divided into groups of six were injected intravenously with 0.1 per cent solution of 1-epinephrine or 1-nor-epinephrine (1-arterenol) as the hydrochloride in physiologic saline in order to compare the pulmonary edema produced by these compounds. The amount of pulmonary edema produced was estimated by the increase in the lung weight per 100 gram body weight as compared to the normal ratio in control animals. All animals that failed to succumb were sacrificed with ether one hour later. Guinea pigs that received 0.0015 and .002 mm. 1-epinephrine per kg. body weight died in from 4 to 11 minutes, while those that were given 0.001 mm. per kg. survived. All of the animals, however, showed pulmonary edema. 1-nor-epinephrine given in larger doses was not fatal, but prostrated the animals and caused pulmonary edema. N-(9-fluorenyl)N-ethyl-beta-chlorethylamine, a beta-haloaklylamine adrenergic blocking agent, administered from 10 to 15 minutes prior to the injection of 1-epinephrine or 1-nor-epinephrine, prevented both the toxic symptoms and pulmonary edema caused by these drugs. I. GLAZER.

Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm. II. Historical Development and Methods. Levinson, L., Beakey, J. F., Bresnick, E., and Segal, M. S.: Ann. Allergy **6**: 705, 1948.

A method for evaluating substances used in the symptomatic treatment of bronchial asthma is presented. The degree of protection afforded by these substances against the decrease in vital capacity which follows the intravenous administration of histamine or Mecholyl may be measured by the formula $P = \frac{C - E}{C} \times 100$ where P represents the degree of protection in per cent, C the control drop in vital capacity produced by an injection of the same quantity of bronchospastic agent before the administration of the protecting drug, and E the decrease similarly produced at any given time after the administration of the protecting drug. W.

Bronchiectasis: Its Curative Treatment by Pulmonary Resection. An Analysis of Ninety-Six Cases. Ochsner, A., DeBakey, M., and DeCamp, P. T.: Surgery **25**: 518, 1949.

Ninety-six cases of bronchiectasis treated surgically were analyzed. The average age of the patients was 30 years, the average age of onset was 13 years, and the duration of symptoms averaged thirteen years. The incidence was about equally distributed in both sexes. The precursors of the disease in their order of frequency were: pneumonia, pulmonary abscess, aspiration of a foreign body, influenza, pertussis, and measles. Bronchography was the most important diagnostic aid. Partial or total pulmonary resection was done in each of the ninety-six cases; bilateral operations were done in four patients. Satisfactory results were obtained in 80 per cent of the patients. Among this group, 45 per cent became symptom-free, 22 per cent had minimal symptoms, and 13 per cent were improved but still had moderate symptoms. There were six postoperative deaths; however, the postoperative mortality and complications of pneumonia, emphysema, and bronchial fistula progressively declined due to better evaluation and management of patients, technical surgical advances, the use of antibiotics, and blood transfusions. Conservative treatment was palliative, but never curative. Pulmonary resection is recommended when the disease is neither too mild nor too extensive, provided the patient is less than 55 years of age and there is no medical contraindication. J. S.

Allergy to Molds in Sweden. A Botanical and Clinical Study. Nilsby, I.: Acta Allergologica **2**: 57, 1949.

Daily mold counts were made in Orebro for eighteen months by the plate exposure method. Pronounced seasonal variations were observed. A definite mold season could be ascribed to the period from June to October. The most commonly found molds included Hormodendrum, Penicillium, Pullularia, and yeastlike fungi. Strong winds and fog increased the mold counts. Extensive mold studies were conducted in homes and various working places; e.g., barns, greenhouses, factories, and groceries. There was little variation between the mold count in the average size city and in the surrounding country. Airplane studies revealed that the mold count decreases with increasing altitude up to 1,000 meters, although occasionally molds are present at higher levels. An extraordinary collection of molds was found in clouds. Twenty-three (18 per cent) of 123 patients with bronchial asthma tested intracutaneously with a 1:2,000 dilution of mold extracts showed positive reactions. One hundred twenty-seven (10 per cent) of 1,250 allergic patients reacted positively to one or more molds. Passive transfer tests were positive in all instances where they were attempted. The author reports a significant discrepancy between positive cutaneous reactions and positive results to provocation tests (nasal, conjunctival, and bronchial). No correlation between dust and mold allergy could be demonstrated. H.

Mediastinal Emphysema Occurring During an Acute Paroxysm of Bronchial Asthma. Grossman, J. W., and Cramer, O. S.: Radiology **52**: 705, 1949.

Mediastinal and subcutaneous emphysema of the neck and anterior chest wall occurred in a young woman during an acute paroxysm of bronchial asthma. Twenty-seven similar cases have been recorded previously in the literature. Recovery was complete. The mechanism of this infrequent complication of bronchial asthma is discussed. J. S.

Dermatology

Importance of Inhalant Allergens in Atopic Dermatitis. Tuft, L.: J. Invest. Dermat. **12**: 211, 1949.

Fifty-four cases of atopic dermatitis are reviewed and the etiologic factors analyzed. Eighty-five per cent of the group showed moderate or markedly positive reactions to house dust. There was also a high percentage of positive reactions to pollens. Mold reactions were insignificant; dander reactions, except for feathers, were uncommon. Four cases are presented to indicate the improvement which can be obtained by environmental changes and autogenous dust or pollen therapy where indicated. Pollens were second only to house dust in provoking exacerbations of atopic dermatitis. Since the areas involved in atopic dermatitis are usually covered by clothing, it must be presumed that dust acts by inhalation rather than by direct contact. Flare-ups from wool may be either specific or nonspecific. When a positive skin test reaction to any inhalant is obtained, the author suggests that the substance be eliminated from the environment. The author concludes that in older children and adults inhalants may be just as important as causative factors in atopic dermatitis as they are in asthma. Atopic dermatitis is designated as "asthma of the skin." R. WISEMAN.

A Study of Atopic Eczema. I. Further Observations on Allergy to Human Dander. II. Cutaneous Reactions to Eczema Scales. Simon, F. A.: Ann. Allergy **6**: 584, 1948.

Among fourteen patients with atopic eczema whose ages ranged from 2 months to 36 years, eleven showed positive reactions to patch tests with human dander. On a regime of dander avoidance, four of these showed definite improvement, one cleared completely, and six showed slight but temporary improvement. Three patients who failed to react to dander were not benefitted by this regime. Eczema scales from some patients possessed the property of producing eczematous reactions of varying degrees on other patients. Among twenty-four eczematous patients patch tested or scratch patch tested on normal skin with the most active scales, positive reactions were obtained in eight of sixteen who were less than 4 years of age, and in three of eight who were more than 9 years old. Among twelve noneczematous controls similarly tested, ten showed negative reactions, one a questionable reaction, and one a slightly positive reaction. Patch tests performed simultaneously with human dander on the same patients and on controls failed to parallel the results with eczema scale. It appears that the allergen present in these scales is not identical with the human dander allergen. W.

Contact Systemic Penicillin Reactions Associated With Oral and Nasal Inhalators. Goldberg, L.: Ohio State M. J. **45**: 1078, 1949.

Fourteen cases of contact and/or systemic reactions to penicillin administered by means of inhalators were observed within a short period of time. The reactions on the face were similar to contact dermatitis caused by cosmetics. The systemic reactions included generalized pruritus, urticaria and the erythematovesicular eruption of the trichophytid type. Although induced sensitivity to penicillin may be temporary, it is quite possible that repeated mild reactions from sources such as inhalators may be missed and eventually lead to more serious reactions such as occur with the sulfonamides, Atabrine, and other drugs. Because of their wide and uncontrolled use, penicillin inhalators should carry warnings of the possibility of sensitization reactions. F.

The Immediate Wheal and the 24-48 Hour Tuberculin Type Edematous Reactions to Trichophytin. Jillson, O., and Huppert, M.: J. Invest. Dermat. **12**: 179, 1949.

Five allergic and six nonallergic patients infected with *Trichophyton rubrum, T. mentagrophytes,* or *Epidermophyton floccosum* were tested intracutaneously with a 1:30 dilution of trichophytin. All showed immediate wheal reactions and only one developed a tuberculin type of reaction. In each case, at least one of the following factors was present: atopy, *T. rubrum* infection, or recurrent lymphangitis.

Twelve patients who responded with a tuberculin type of reaction (papule) were given weekly intracutaneous injections of 0.1 c.c. trichophytin 1:30. In each case, the tuberculin type sensitivity was abolished after from four to twenty-three injections. The urticarial type of sensitivity persisted in two patients who manifested it before treatment was started and, in three additional cases, it appeared at about the time tuberculin type of sensitivity disappeared. In some cases, an intense delayed edematous type of reaction occurred after each injection. The following conditions favor the production of the wheal type of sensitization to trichophytin and indicate the importance of time and a constant supply of antigen in these mechanisms: (a) *T. rubrum* infections are persistent, chronic, and recalcitrant dermatoses; (b) lymphangitis causes stasis and possible trapping of the antigen; (c) atopy enhances the production of reagins; and (d) repeated injections of trichophytin. It is suggested that, in the process of sensitization, fixed tissue antibodies are first produced and circulating antibodies which may be passively transferred are formed later.

I. Glazer.

The Cellular Content of Exudates From Eczematous and Toxic Patch Test Reactions. Nexmand, P. H.: J. Invest. Dermat. **13**: 85, 1949.

Nine patients with allergic contact-type reactions were patch tested with specific contactants (turpentine, balsam of Peru, crude coal tar, ammoniated mercury, wood tar, chrysarobin, and resorcin). A primary irritant (5 per cent phenylmercuric triethanol ammonium acetate) was applied in a similar fashion on nine other subjects. After forty-eight hours, smears of the fluid contained in the vesicles and bullae were stained with Giemsa's stain and differential counts were made. Plasma cells were absent. In the smears from the nonspecific reactions, many polymorphonuclear leukocytes with vacuoles and fragmentation of nuclei were found. Mononuclear cells (lymphocytes, monocytes, and transitional cells) were generally abundant in the specific reactions, whereas polymorphonuclear leukocytes were the predominating cells in the nonspecific reactions.

I. Glazer.

Reactions to the Local Use of Thephorin. Ellis, F. A., and Bundick, W. R.: J. Invest. Dermat. **13**: 25, 1949.

Fourteen of fifty patients with chronic pruritic dermatoses treated locally with Thephorin lotion or ointment for an average period of fifty days became worse or developed a local reaction to the drug. Only five patients were patch tested with the ointment or lotion and all showed positive reactions. Three of these cases also had positive reactions when patch tested with an aqueous solution of Thephorin. The authors warn against the indiscriminate use of this drug.

B. S.

Ragweed Dermatitis. Therapy by the Oral Route. Slater, B. V., Norris, J. L., and Francis, N.: Ann. Allergy **6**: 594, 1949.

Two cases of contact dermatitis attributed to ragweed pollen are presented. The first patient, a 40-year-old gardener, had a recurrent dermatitis which lasted from May to January for several years. Patch testing with ragweed oil yielded markedly positive reactions. When this patient was treated with ragweed oleoresin orally, he remained free of dermatitis for a year. The second patient showed positive reactions to ragweed, golden rod, and metallic silver. He had exacerbations of eczematous lesions in September, October, or November for several years. The oral administration of ragweed oleoresin in incorrect dosage caused a marked flare-up in his lesions. Visits to mountainous areas during the pollen season produced considerable relief of symptomatology. Exacerbations of the skin lesions often followed contact with substances other than ragweed. It was thought that ragweed was the prime offender and that the other substances were of secondary importance. W.

Contact Dermatitis Due to Procaine (A Common Occupational Disease of Dentists). Laden, E., and Wallace, D.: J. Invest. Dermat. **12**: 299, 1949.

Ten dentists, all suffering from chronic dermatitis involving the hands, were patch tested with various groups of local anesthetics. Nine of the ten patients showed positive reactions to drugs of the procaine group. Seventy-five per cent of the subjects reacted to all the compounds of this type although several had never been exposed to some of the drugs, such as Larocaine hydrochloride or Tutocaine hydrochloride. Drugs such as Metacaine hydrochloride and Nupercaine hydrochloride whose side chain contained an amino nitrogen but whose nucleus differed markedly from p-amino benzoic acid, yielded negative patch reactions. Patch tests with alkyl esters of p-amino-benzoic acid whose compounds have the same nucleus as procaine but whose alcoholic side chain does not contain an amino nitrogen were negative in 90 per cent of the cases. One patient previously exposed to Butesin showed a positive patch reaction. The authors concluded that hypersensitivity to one member of the procaine group usually indicates that hypersensitivity to all the members of the group will develop. When either the nucleus or side chain of these compounds is changed, the sensitizing properties are altered.

R. WISEMAN.

Exfoliative Dermatitis From Contact With DDT. Higgins, E., and Kindel, D.: J. Invest. Dermat. **12**: 207, 1949.

Following the weekly use of DDT as an insecticide in his bedroom, the patient developed a generalized rash. He showed erythroderma of the skin with lichenification, areas of scaliness, and petechia-like pin-point macules. The patient improved rapidly under conservative treatment and subsequently was patch tested with DDT and thirteen other compounds structurally related to DDT. Positive tests were obtained with DDT and two similar compounds. Tests were negative with both solvents. After several months, patch reactions to crystalline DDT were negative, but a positive reaction was obtained with one of the analogues. In view of the wide use of DDT and the paucity of reactions from it, this toxicant appears to have a low sensitizing index.

R. WISEMAN.

An Evaluation of the Patch Test Based on Experimental Findings. Grolnick, M.: Ann. Allergy **7**: 368, 1949.

Experimental studies in sensitization of the skin of humans indicated that the patch test may be a means of provoking sensitization of the nonsensitive

individual. It was also evident that excitants can remain fixed in the skin for relatively long periods of time. To avoid the hazards incident to the clinical implications of these findings, the following precautions should be observed in the performance of patch tests: (1) The nonsensitizing concentrations of contactants should be known. (2) Tests with the same or related excitants should not be repeated under certain conditions. (3) Patch tests should not be applied during the active phase of a dermatitis or a recently subsided dermatitis. (4) A patch test with the specific excitant may produce the generalization of a localized active dermatitis. (5) Local testing in previously involved areas may give nonspecific reactions which are not of etiologic significance. *Author's Summary.*

Contact Dermatitis Due to Phenolphthalein. Skinner, L. C., Jr.: Arch. Dermat. & Syph. **59**: 338, 1949.

While in an army hospital, a soldier was given several alcohol back rubs with a solution containing 70 per cent ethyl alcohol, phenolphthalein, and tincture of cudbear as a coloring agent. Phenolphthalein had been added to discourage the use of the alcohol as a beverage. A week after the initial back rub, the patient developed a severe erythematovesicular eruption over his entire back. Patch tests performed with material containing phenolphthalein gave positive reactions. B. S.

Otorhinology and Ophthalmology

A Study of Ciliary Activity in the Respiratory Tract of Animals. Ballenger, J. J.: Ann. Otol. Rhin. & Laryng. **58**: 351, 1949.

The effect of marked hypersensitivity on the ciliary activity of the respiratory tracts of animals was investigated. Female rabbits were sensitized with subcutaneous injections of horse serum administered every five to seven days. The development of an ulcer (Arthus phenomenon) after the sixth or ninth injection was accepted as a criterion of sensitivity. The sensitized animals were sacrificed and transverse sections of trachea were immersed in 50 per cent, 17 per cent, and 10 per cent horse serum and in 0.85 per cent saline solution. These sections were removed from the bath from time to time and examined under the ultropak microscope for vigor of ciliary activity. Sections of trachea from nonsensitized rabbits, used as controls, failed to show any diminution of ciliary activity when immersed in 0.85 per cent saline, 10 per cent horse serum, and 17 per cent horse serum. However, the 50 per cent horse serum solution appreciably slowed down ciliary motion. Tissue excised from the group of sensitized animals and immersed in the same horse serum baths did not show any decrease in ciliary activity. The tracheal cilia of nonsensitized animals fatally shocked with an overwhelming dose of histamine 1:1,000 maintained their normal activity. When histamine 1:1,000 was dropped on the excised tracheal tissue of horse serum-sensitive rabbits, the vigor of the ciliary activity was not impaired.

It was concluded that ciliary function is not acutely depressed in nonsensitized or sensitized rabbits when the antigen (horse serum) is introduced. Similarly there is no qualitative ciliary depression in sensitized or nonsensitized animals following either an overwhelming intravenous dose of 1:1,000 histamine or the local application of 1:1,000 histamine directly upon the cilia. C.

Introduction to Studies on the Common Cold. Dochez, A. R.: Bull. New York Acad. Med. **25**: 528, 1949.

Certain gram-positive and gram-negative cocci, diptheroid bacilli, and other organisms have repeatedly been found to be associated with outbreaks of the common cold. A specific causative relationship between these organisms and the common cold is difficult to establish because of their constant presence in the respiratory flora of healthy individuals. In order to evaluate the pathogenic importance of these organisms, a group of subjects whose normal nasopharyngeal flora was well known were studied after they had contracted colds. During the early stages of the cold no new organisms appeared. Whenever there was increased bacterial activity, it occurred late and was associated with some complication that had developed. It was concluded that the common pathogens of the nasopharynx are not the initiating agents of infection of the respiratory tract and that they act principally as secondary invaders in an inflammatory process induced by an unknown primary agent. Studies on chimpanzees and human subjects showed that inoculation of bacteria-free material obtained from individuals with typical colds resulted in typical colds which could be transferred from human to human in series. The virus etiology of the common cold was thus established.

Immunization with a living virus vaccine was not successful. This was to be expected because of the lack of an enduring immunity following a spontaneous attack of the common cold. C.

Research on the Common Cold. Topping, N. H.: Bull. New York Acad. Med. **25**: 530, 1949.

Unfiltered nasal washings obtained from individuals within 24 hours after the onset of cold symptoms produced signs and symptoms of minor upper respiratory infection in 5 of 5 volunteers, within 36 or 48 hours. The nasal washing from one of these was inoculated into embryonated hen eggs and several substrains obtained. One of these substrains produced 100 per cent illness in 14 volunteers. Sixth and seventh passage allantoic fluids containing this substrain produced moderately severe illness in 15 of 16 and in 14 of 16 volunteers, respectively. Microscopic studies failed to reveal bodies suggestive of bacteria or the large viruses. Electron microscopic examinations showed characteristic particles of the same general size as viruses of the influenza type, but readily distinguishable from them. C.

Miscellaneous Allergies

Serological Studies in Rheumatic Fever. II. Serum Complement in the Rheumatic State. Fischel, E. E., Pauli, R. H., and Lesh, J.: J. Clin. Investigation **28**: 1172, 1949.

Complement fixation studies were carried out on fifty normal individuals and on fifty patients with acute rheumatic fever. Quantitative determinations were made using a spectrophotometer technique. Normal complement levels were 37.7 + 3.9 units per milliliter. "Forty-five of fifty patients with rheumatic fever had an elevation of the serum complement above 50 units per milliliter of serum at the onset of the attack or shortly thereafter. Two patients presented a low complement which gradually became normal." In two patients who died the levels were low, not an uncommon finding preceding death from other causes. Since allergic reactions may occur without any observable diminution in complement, the allergic hypothesis for the develop-

ment of rheumatic fever is not negated by the present findings. The possible factors responsible for raising complement levels in rheumatic fever are discussed. K.

Antihistamines in Bronchial Asthma. Herxheimer, H.: Brit. M. J. **2**: 901, 1949.

Bronchial spasm was induced in normal individuals and asthmatics by the aerosolization of spasmogenic substances, such as histamine acid phosphate, acetyl-B-methylcholine chloride, and allergenic extracts (pollens, mixed inhalants). The degree of spasm which resulted was measured by diminution of the vital capacity. When histamine aerosol was administered to sixteen normal subjects, three showed no decrease in vital capacity, five showed a decrease of only 5.9 per cent, and eight showed a decrease of from 12 to 26 per cent. With acetylcholine, only two of fourteen normal subjects showed a decrease in vital capacity. In asthmatics, however, histamine and acetylcholine frequently produced an almost immediate marked decrease in the vital capacity. Phenergan, Neoantergan and Pyribenzamine aerosol suppressed the mild spasm (vital capacity depressed 30 per cent or less) induced by histamine, acetylcholine, and allergenic extracts. When the vital capacity had been reduced more than 50 per cent, the antihistamine drugs failed to afford protection. Asthmatic patients required larger amounts of the antihistaminics than normal subjects for protection against induced symptoms. H.

Unusual Reactions to Ant Bites. Morehouse, C. H.: J. A. M. A. **141**: 193, 1949.

A very severe reaction consisting of generalized urticaria, stertorous breathing, and signs of impending shock occurred shortly after a series of ant bites. The patient, a soldier, had had similar attacks after being bitten by an unknown insect and after the administration of gas gangrene antitoxin. Epinephrine 0.4 mg. and oxygen afforded only slight relief. Pyribenzamine administered orally produced some relief. Intravenous procaine therapy resulted in almost instantaneous relief from symptoms. F.

Acute Polyarteritis Nodosa in Childhood. Taylor, A. W., and Jacoby, N. M.: Lancet **2**: 792, 1949.

A 7-year-old boy, who had been treated with sulfonamides for a sore throat developed edema of the face, nausea, and vomiting a few days later. This was followed by multiple spontaneous hemorrhages in the orbits and soft tissues around the eyes, epistaxis, hematemesis, purpura of both feet and ankles, and absolute anuria. The blood count revealed 86 per cent polymorphonuclear cells but no eosinophilia. No mention was made of personal or family history of allergy. Death occurred on the sixth day. Postmortem studies showed polyarteritis nodosa in most tissues with severe involvement of the kidneys and spleen. H.

The Shwartzman Phenomenon With Penicillin: Report of a Case. Boelter, M., and Hatoff, A.: Arch. Pediat. **66**: 335, 1949.

A reaction of the Shwartzman phenomenon type was observed in a 10-year-old girl suffering from an aspiration pneumonia. The patient had received penicillin in oil intramuscularly every twelve hours for nine days. On

the tenth day, treatment was changed to acqueous penicillin intramuscularly. After two doses the patient complained of pruritis and developed 16 to 18 indurated, nontender urticarial wheals on the buttocks. Each of the wheals surrounded a puncture site where penicillin in oil had been administered. The child began to complain of severe pain following each injection of penicillin. Slight ptosis of the right eyelid supervened and her temperature rose to 101.2° F. On the day following the onset of symptoms, a confluent erythema developed over the entire buttocks and an area of induration could be palpated. Recovery occurred following the withdrawal of penicillin. F.

Anaphylaxis

Toxemia as a Stimulation Factor in the Production of Antibodies. Studies on Precipitin Production in the Dog. I. The Use of Egg White. Mann, L. S., and Welker, W. H.: J. Infect. Dis. **85**: 146, 1949.

Precipitins against egg protein and ox albumin were successfully produced in dogs. The technique employed consisted of the injection of ox albumin adsorbed on aluminum hydroxide cream followed at specified intervals by the injection of 1 per cent egg white solution. The precipitin tests were made by the layer method with various antigen dilutions. The toxic effect of the intravenously administered egg white was apparently responsible for the precipitin production. No regularity was observed in the appearance or disappearance of the ox albumin precipitins. F.

Toxemia as a Stimulation Factor in the Production of Antibodies. Studies on Precipitin Production in the Dog. II. The Use of Ricin. Mann, L. S., and Welker, W. H.: J. Infect. Dis. **85**: 151, 1949.

Precipitins against ox albumin were successfully produced in dogs by an intramuscular injection of ox albumin fixed on aluminum hydroxide cream followed by a single subcutaneous injection of 0.0005 mg. of ricin per kg. Precipitins were present for from 3 to 45 days after the injections. Subcutaneous injections of larger doses of the toxic ricin, against which resistance had developed as a result of the previous injection, failed to provoke further precipitin formation. This indicated that the precipitin formation was a direct result of the toxic state rather than the result of stimulation by a foreign protein formed by the union of the toxin and the antigen. F.

Pharmacology, Physiology, and Pathology

Local Sweating in Man Induced by Intradermal Epinephrine. Sonnenschein, R. R.: Proc. Soc. Exper. Biol. & Med. **71**: 654, 1949.

Twenty-one of thirty subjects injected intracutaneously on the forearm with 0.1 c.c. of a 1:10,000 or a 1:100,000 solution of epinephrine manifested definite local sweating. This response varied in intensity among subjects and in individuals tested on different days. The response was similar in both sexes and among different races. It began a minute following the injection and involved the area of vasoconstriction with its lymphatic spread. It began to diminish twenty minutes later. Among the nine subjects who showed no significant response, five developed marked sweating following the injection of acetylcholine or nicotine. One subject had apparent inhibition of sweating following epinephrine. Pretreatment of the skin by the intracutaneous injection of 0.4 c.c. Atropine sulfate 1:100,000 or tetraethylammonium chloride 1:100 had no significant effect on the response to epinephrine. Procaine hydrochloride 1:100 caused slight to marked inhibition. Dibenamine intro-

duced into the skin of subjects by ion transfer inhibited epinephrine 1:1,000,000 but only partially inhibited epinephrine 1:100,000 and had no significant effect on the response to acetylcholine 1:1,000,000. The results indicated that at least some sweat glands of certain individuals are sensitive to the direct action of epinephrine. The significance of these findings is unknown. I. GLAZER.

The Effect of an Antihistamine Agent on Various Whealing Phenomena. Friedlaender, S., and Friedlaender, A. S.: Revista mex. de Alergologia **1**: 14, 1949.

Pyribenzamine solutions, varying from 1 to 5 per cent, were applied to scratch sites on dermographic subjects. The whealing response induced by a stroke across the area was found to be inhibited at the pretreated sites, especially when the higher concentrations of Pyribenzamine were used. Skin sites prepared with Pyribenzamine solutions were tested twenty minutes later with solutions of histamine, bee venom, codeine, Atropine and eserine. There was about 50 per cent inhibition of reactions at the pretreated sites containing 0.05 to 0.1 mg. of Pyribenzamine per c.c. Pilocarpine reactions were reduced to a comparable degree at sites containing higher concentrations of Pyribenzamine. Acetycholine and mecholyl reactions were relatively unaffected by the pretreatment of sites. Pyribenzamine exerted an inhibitory effect on whealing regardless of the agent responsible for its production. When whealing was not a significant part of the response, as in case of acetylcholine and Mecholyl reactions, inhibition was not as prominent, suggesting that the action of antihistaminics is primarily on capillary permeability rather than on vasodilatation.

Solutions of Pyribenzamine 1:1,000 and procaine 1:200, which were found to produce gross cutaneous anesthesia for approximately the same period of time, were injected intracutaneously into normal subjects. The inhibition of histamine, codeine, Atropine, and eserine wheals at Pyribenzamine sites was the same after 5 and 60 minutes. Procaine inhibited histamine and eserine wheals less effectively at 5 minutes and relatively little at 60 minutes. Atropine and codeine wheals were unaffected by pretreating the sites with procaine. Pilocarpine wheals were unaffected by both solutions. The authors conclude that the antiwhealing effect of Pyribenzamine is not related to its anesthetic properties.

The pretreatment of skin sites by the iontophoresis of from 1 to 5 per cent Pyribenzamine solution resulted in a subsequent inhibition of wheals induced by histamine 1:100,000 iontophoretically. This procedure was less effective against Atropine, eserine, and stronger solutions of histamine and ineffective against the flushing reactions of acetylcholine. The latter reaction was inhibited by pretreating the skin site with Atropine by iontophoresis. Attempts to extract a whealing substance from combined histamine Pyribenzamine sites by reversed electrophoresis were unsuccessful. Attempts to transfer Pyribenzamine itself by reversed iontophoresis were unsuccessful. It is assumed that the antihistaminic agent in some way holds histamine at the initial site. B. S.

Histamine Metabolism in Pregnancy. Kapeller, A. R.: Lancet **2**: 745, 1949.

Determinations of the histamine content of the plasma and the blood cells and simultaneous determinations of histaminase activity of the serum were made in 91 pregnant patients in various stages of pregnancy and in 8 nonpregnant patients. The sera of all the pregnant patients showed strong histaminase activity. In mild toxemia histaminase activity was unchanged,

but in severe toxemia it was definitely decreased. In the later stages of labor, there was also a decline in histaminase activity. Histamine was present in the cells of pregnant patients in amounts comparable to that present in the blood cells of the nonpregnant subjects. In mild toxemia the histamine content of the plasma was greater than in nonpregnant patients. In severe toxemia the histamine content of the cells was low, but the histamine content of the plasma was high. During labor the histamine content of the blood was high. H.

Effect of Adrenalectomy on Eosinophil Response of Rats Infected With Trichinella Spiralis. Larsh, J. E., Jr., and Nichols, J.: Proc. Soc. Exper. Biol. & Med. **71**: 652, 1949.

Rats and white mice were infected with *Trichinella spiralis* and one month later were reinfected with the same parasite. Only a very moderate rise occurred in their eosinophil counts. Rats showed a rise from a normal of 1 per cent to 3 per cent and mice from a normal of 3 per cent to 10 per cent. Nineteen rats were then adrenalectomized and kept alive by careful maintenance of their electrolyte balance. Eleven of these animals were then infected with *T. spiralis.* They failed to show a significant rise in their eosinophil counts. R. WISEMAN.

Effect of Antihistamine on the Localization of Trypan Blue in Xylene-Treated Areas of Skin. Rigdon, R. H.: Proc. Soc. Exper. Biol. & Med. **71**: 637, 1949.

Thenylene or Pyrrolazote was administered parenterally to rabbits both before and after the application of xylene to numerous areas of the skin. Trypan blue was then injected intravenously. No difference was noted in the localization of trypan blue among the animals receiving antihistaminics and the control animals. The intensity of hyperemia which resulted from the application of xylene was not affected by the drugs. Areas of skin where antihistaminics had been injected intradermally showed local concentration of the dye. It was concluded that neither the hyperemia which follows the local application of xylene nor the localization and concentration of trypan blue in xylene-treated areas of skin were affected by the antihistaminics used. R. WISEMAN.

The Administration of Histamine During Pregnancy: Apparent Lack of a Clinical Oxytocic Effect With Small Doses. McElin, T. W., and Horton, B. T.: Am. J. M. Sc. **218**: 432, 1949.

No true oxytocic effect was noted in any of fifteen pregnant women who received histamine either intravenously or subcutaneously in doses as high as 2.75 mg. Treatment was given in every stage of pregnancy and in some cases it was continued throughout the entire period of gestation. In only one instance was there a possible untoward effect; a primigravida, aged 29 years, developed slight bleeding twelve hours following a subcutaneous injection of only 0.137 mg. of histamine. Post-partum bleeding was not observed in any of the cases. These findings are contrary to those previously recorded in the literature. F.

The Pharmacologic Actions of Intravenous Procaine as an Analgesic Agent. Isenberger, R. M.: Anesthesiology **10**: 343, 1949.

The intravenous administration of procaine produces moderate analgesia, relief of pruritus, and increased peripheral circulation. Because of its prompt

hydrolysis and its rapid disappearance from the blood stream, procaine should be administered in low concentrations. Toxic reactions following intravenous procaine are dependent upon the speed of injection, the total dose administered and the concentration of the solution used. The author states that individual idiosyncrasy is not uncommon. H.

Hydrolysis of Choline Esters in the Presence of Adrenalin. Benson, W. M., and Meek, W. J.: Am. J. Physiol. **158**: 327, 1949.

The hydrolysis of acetylcholine beta-methyl-acetylcholine and benzylcholine by cholinesterase was inhibited by the presence of adrenalin. Cholinesterase from various sources, such as the caudate nucleus of the hog and dog and the parotid gland of the hog, was used in the experiments with no variation in the order of magnitude of inhibition. Depression of the enzymatic activity was shown to be in direct ratio to the concentration of adrenalin. F.

Skin Reactions. XVI. Comparison of Antihistaminic Action of Pyribenzamine and Epinephrine Introduced Into Human Skin by Electrophoresis. Abramson, H. A., Grosberg, S.: Ann. Allergy **7**: 325, 1949.

When epinephrine 1:10,000 was introduced into the skin by electrophoresis, the initial irritation which followed disappeared within a few minutes and a clearly blanched area was observed. The blanched area was surrounded by a flare. Histamine 1:50,000 was then introduced with a rectangular electrode, half of which covered the epinephrine site. A distinct histamine wheal was produced. The portion of the histamine wheal which extended beyond the blanched area persisted, while that part within the epinephrine site disappeared within forty-five minutes and the blanching returned. This "restoration effect" of epinephrine was more pronounced when higher concentrations of both drugs were used. Pyribenzamine hydrochloride solution also inhibited reactions to histamine. Weight for weight, epinephrine was approximately 1,000 times more effective than Pyribenzamine as an antihistaminic in the present experiment. W.

Experimental Determination in Human Subjects of the Duration of "Antihistaminic" Activity of Orally Administered Compounds. Perry, D. J., and Hearin, D. L.: J. Invest. Dermat. **13**: 29, 1949.

The threshold whealing response to histamine, introduced by electrophoresis, was determined in forty-five subjects. The group was equally divided and given either 50 mg. of tripelennamine hydrochloride, 50 mg. of diphenhydramine hydrochloride, or two tablets of Hydryllin orally. Subsequently the threshold whealing reactions to histamine were determined at hourly intervals for five hours. It was found that, in fourteen patients equally divided in the three groups, there was no evidence of antihistaminic activity in one hour. The average antihistaminic activity of all three drugs was maximal two hours after their administration. This was maintained at three hours, declined at four hours, and disappeared at five hours. All three drugs demonstrated similar curves of histamine antagonistic activity. It was concluded that the doses of the antihistaminics used above be given orally at four-hour intervals in order to maintain an active level of the drug. B. S.

Antihistamines as Antidote Against Histamine-like Effect of Curare Preparations. Poulsen, H.: Nord. med. **41**: 623, 1949.

The undesirable side effects of curare preparations used in psychiatric shock treatments and in surgical anesthesia are partly due to the histamine-

like action of the drug. The intravenous administration of antihistamine drugs prior to the injection of curare in anesthesia or shock treatment reduced the incidence of side effects in 155 of 330 patients and, in many cases, prevented such effects completely. In electroshock therapy, antihistamine drugs counteract hypersecretion in the respiratory tract, bronchospasm, and bronchiolspasm which result from the administration of curare. In surgical anesthesia, the antihistamine drugs also counteract capillary oozing in the operation field. H.

Miscellaneous

Failure of Sensitized Sheep Cell Agglutination to Clarify the Diagnosis of Rheumatic Disease. Miller, J. E., Lynch, E. R., and Lansburg, J.: J. Lab. & Clin. Med. **34**: 1216, 1949.

Some investigators have reported that the sera of patients suffering from active rheumatoid arthritis agglutinated sheep cells sensitized with rabbit anti-sheep cell sera in much higher titers than they agglutinated plain sheep cells. The authors tried to confirm this work in twenty-one rheumatoid arthritics and twenty-three control subjects. They failed to observe any significant difference between sera from rheumatoid arthritics and from the controls. These workers suggest that the previous findings were probably due not to a specific antibody but to the presence of some nonspecific factor in the serum. They further suggest that this nonspecific factor might be an increase in some serum component, possibly a globulin, which caused an alteration in the physicochemical equilibrium of the test mixture. K.

The Distribution and Storage of Blue Antigenic Azoproteins in the Tissues of Mice. Kruse, H., and McMaster, P. D.: J. Exper. Med. **90**: 425, 1949.

Two blue azoproteins were prepared from a blue dye in such a form that no free blue dye was present to be mistaken for the azoprotein. The method of preparation was described in detail. Mice tolerated the azoproteins well even in large dosage but could readily be thrown into anaphylactic shock by subsequent injections. It was found that one diffusible dye used, Echt-Säure-Blau-B, was not stored intracellularly as granules. When this dye was injected in mice in aqueous form it remained in the tissues up to three hours and was excreted in the bile and urine. Retention of color following the injection of this azoprotein indicated that a dye-protein linkage existed. When Echt-Säure-Blau-B azoglobulin was administered in the tail veins of mice, no color appeared in either the bile or urine and, in three to five minutes, blue matter could be discerned in the Kupffer cells of the liver and in other reticuloendothelial cells. In three to thirty minutes, tissues generally became blue, the intensity increasing progressively up to the forty-eighth hour at which time the visible blue of the plasma disappeared. The final distribution of antigenic dye was like that of finely divided particulate matter. The Kupffer cells of the liver, and sinus and reticular cells in lymph nodes, especially the great mesenteric node, were particularly active in taking up the dye in mice, but vascular endothelial cells and other parts of the reticuloendothelial system also picked up the antigen. That the blue dye seen in the Kupffer cells of the liver was actually stored antigen was demonstrated by complement fixation. Antigenic activity of liver suspensions was greater than antigenic activity of the blood.

The distribution of antigenic dye following both intracutaneous and intravenous injection was described in detail. Dye was found in all organs except the brain. It was confined to the cytoplasm and was never in the

nuclei. Antigen concentration was nearly as intense in the kidney tubules as in the liver and mesenteric lymph nodes. It was also concentrated in muscle cells of the uteri, in spleen, omentum, lungs, and in smooth muscle all through the body. It was found in peripheral lymph nodes, in mesenteric nodes, in liver, and in histiocytes and other connective tissue. The distribution of azoprotein dye after intraperitoneal injection was eventually the same as that following intravenous injection. Blue color has been observed in mice as long as three and a half months after the injection of Echt-Säure-Blau-B azoprotein. The fading at this time indicated the slowness of the breakdown of the antigen. Only traces of antigen were found in the blood by the twelfth day following intravenous injection but traces continued for many more days. It is suggested that possibly there is a slow output of antigen from that stored in the reticuloendothelial cells as the latter slowly lose their color.

A second azoprotein made from horse serum protein and dye "T-1824" could not be used for tests of retention of antigen because the dye itself was not rapidly excreted. However, the distribution and behavior of this compound confirmed the findings with Echt-Säure-Blau-B azoprotein and proved a superior antigen tracer compound because of its intense color. K.

Eczema Vaccinatum: Rapid Recovery Following Treatment With Aureomycin. Perry, G., and Martineau, P. C.: J. A. M. A. **141**: 657, 1949.

A 2-year-old child with a history of atopic eczema since infancy developed generalized vaccinia. The condition occurred four days after the patient had played with another child who had an encrusted smallpox vaccination scar. Umbilicated vesicles first appeared on the neck and rapidly spread to the face, to the anterior aspect of the upper chest, the extensor surface of the arms, and the anterior aspect of the thighs. There was generalized lymphadenopathy. The temperature rose to 104.8° F. and the white cell count to 34,000. Biopsy of a vesicle taken on the fourth day of illness was histologically typical of vaccinia and the reaction to Paul's test was positive for the vaccinia virus. Penicillin was administered for two days without improvement. Aureomycin was then substituted and improvement was noted within twenty-four hours. Within seventy-two hours the temperature returned to normal. Complete recovery ensued and the patient was discharged on the eleventh hospital day. F.

Pseudoreactions to the Tuberculin Patch Test. Vollmer, H.: Am. J. Dis. Child. **78**: 302, 1949.

Pseudoreactions to the tuberculin patch test, while rare, are particularly prone to occur in atopic individuals. Many are caused by improperly concentrated tuberculin produced during the war years. Pseudoreactions may be distinguished from true reactions by reading the test again from four to seven days after removal of the patch. Pseudoreactions are maximal about the time the patch is removed, while true reactions increase beyond this time and usually persist for a week. K.

Failure of Adrenocortical Extract to Modify the Immunity Acquired by Intact Mice Through the Use of Pneumococcal Vaccine. Vollmer, E. P., and Samsell, J. E.: Endocrinology **45**: 204, 1949.

Adrenocortical extract appears to have no effect upon the resistance of Swiss mice to pneumococci. Experiments were done varying the dosages of the adrenocortical extract and of the immunizing and challenging inocula over a wide range. There was no evidence of any change in the immunity of the animals over control groups. F.

The Diagnostic BCG Test. Ustvedt, H. J., and Aaronsen, A.: Acta tubere. Scandinav. **23**: 1, 1949.

Tuberculin tests may yield negative results in the presence of tuberculosis and occasionally give nonspecific positive reactions in the absence of the disease. The authors believe that increasing the tuberculin concentration above 1 mg. in the Mantoux test increases the incidence of nonspecific reactions. They suggest that in tuberculin-negative patients with tuberculous infection, or in patients who show a negative Pirquet reaction and a positive Mantoux, the diagnostic BCG test should be made. This test is performed by making two punctures in the skin through a drop of BCG containing 20 mg. per c.c. The reaction at the test site is read six days later. A specific reaction consists of distinct papules at the test site and is designated "positive early reaction to BCG." H.

Failure of Antihistamine Drugs to Inhibit Hyaluronidase in Vitro. Moynahan, E. J., and Watson, D.: Nature **163**: 173, 1949.

The enzymatic activity of hyaluronidase, prepared from rabbit and rat tests, was measured by a viscosimeter. Solutions of Antistine, Benadryl, Pyribenzamine, and Neoantergan in concentrations of 0.003, 0.033, and 0.33 per cent were tested for possible antihyaluronidase activity. There was no evidence that antihistaminics inhibit hyaluronidase in vitro. H.

Toxicity of Drugs Used in Local Anesthetics, With Report of a Fatal Case. McCulloch, J. R.: M. J. Australia **2**: 416, 1949.

A brachial flexus block and infiltration of the paravertebral spaces with a mixture of procaine 1:200 and Nupercaine, resulted in a fatality in a 28-year-old woman. After 90 c.c. containing less than 25 mg. of Nupercaine and less than 0.5 Gm. of procaine had been given, the patient suddenly became unconscious and died. Postmortem studies failed to reveal the cause of death. The literature on anesthetic deaths is reviewed. H.

The Etiology of Erythema Nodosum. Roddy, R. L.: J. Pediat. **34**: 338, 1949.

Erythema nodosum is frequently associated with tuberculosis, rheumatic fever, streptococcal infection of the upper respiratory tract, and following the administration of sulfonamides and diphtheria toxoid. Its association with coccidioidomycosis and the injection of Frei antigen has also been reported. The authors conclude that erythema nodosum is probably a reaction to a sensitizing agent in an individual already sensitized. J. S.

Antihistamine Therapy in Thrombophlebitis Migrans. A Case Report. Selecman, F. A., and Miller, E. W.: Surgery **25**: 605, 1949.

A 50-year-old woman with thrombophlebitis migrans was successfully treated with antihistaminics. The patient had had numerous recurrences over a period of twenty-five years and suffered at least one severe pulmonary embolism. The usual forms of therapy were of no avail until one of the antihistaminic drugs was administered orally. Within twenty-four hours there was marked improvement and within a week there was no sign of venous inflammation. The patient remained well for four months following therapy. Allergic studies were not performed. J. S.